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(54) Title: MODIFIED POLYMERIC FILMS

(57) Abstract: A hydroxypropyl methyl cellulose film comprises hydroxypropyl methyl cellulose plasticised with a plasticiser comprising an organic acid or a salt of an organic acid, preferably lactic acid, or an alcohol or salt of an alcohol. The film is safe for human consumption and finds use as a wall material of an ingestible delivery capsule, e.g. containing a dose of a pharmaceutical preparation.

Modified polymeric films

Field of the invention.

This invention relates to films of modified polymeric materials, more particularly of films of the modified cellulose material hydroxypropyl methyl cellulose (HPMC), and uses of such films.

Background of the invention.

Hydroxypropyl methyl cellulose is a synthetic plastics material, which is a modified form of the naturally occurring polymer, cellulose. Films, (or sheets or membranes) of HPMC are available commercially and have various uses, including proposals for use as wall materials of delivery capsules i.e. capsules designed to retain and protect their contents until an intended site of delivery or conditions of delivery are encountered, at which point the contents of the capsules are released. HPMC is suitable for ingestion by humans, so delivery capsules with HPMC walls find the potential use as ingestible capsules, e.g. for the delivery of accurately metered doses of pharmaceutical preparations and dietary supplements, as a possible replacement for gelatin based capsules. See for example, WO 97/35537, WO00/27367 and WO 01/03676.

When producing HPMC films, HPMC is usually treated with a plasticiser in order to impart or improve properties of flexibility to the film. Materials used as plasticisers include polyethylene glycol (PEG), monopropylene glycol, glycerol and also acetins (which are acetates of glycerol).

In a typical method of making a cast HPMC film, HPMC, PEG and water are mixed to produce an aqueous solution, followed by optional deaeration of the solution if a non-aerated film is required. The film is then fed in a controlled manner to the surface of a continuous belt, producing a cast film of desired thickness which is fed on the belt past heating means for drying the film. The dried film is then removed from the belt and wound onto reels.

The present invention concerns novel plasticiser materials for polymeric films, more particularly HPMC films.

Summary of the invention

In one aspect of the present invention provides hydroxypropyl methyl cellulose film, comprising hydroxy propyl methyl cellulose plasticised with a plasticiser comprising an organic acid, or derivative or salt of such an acid.

In another aspect of the present invention provides hydroxypropyl methyl cellulose film, comprising hydroxypropyl methyl cellulose plasticised with an organic alcohol, derivative or salt of such an alcohol.

Suitable organic acids are carboxylic acids, such as mono, di, tri, or tetra or other polyvalent carboxylic acids.

Carboxylic acids according to the present invention include the following:

C1-C6 saturated or unsaturated, straight or branched chain carboxylic acids, with 1,2,3 or 4 carboxyl groups
C1-C6 hydroxy acids with any combination of 1,2,3,4 hydroxyl/carboxyl groups, including beta hydroxy acids (BHA's)
Cyclised acids and cyclised hydroxy acids

Specific examples of acids according to the present invention include the following:

unsaturated carboxylic acids
Adipic acid
Fumeric acid
Fumaric acid
Maleic acid
Proprionic acid

saturated carboxylic acids
Ethanoic acid
Propanoic acid
Butanoic acid
Pentanoic acid
Hexanoic acid

hydroxy acids
Alpha hydroxy butyric acid
Mandelic acid

cyclised acids and cyclised hydroxy acids
Gamma butyrolactone
Gamma valerolactone
Beta propriolactone

In another aspect of the present invention provides hydroxy propyl methyl cellulose film, comprising hydroxy propyl methyl cellulose plasticised with an organic alcohol, derivative or salt of such an alcohol.

Alcohols according to the present invention include C1-C8 substituted or unsubstituted, saturated or unsaturated, straight or branched chain aliphatic alcohols.

Examples of alcohols according to the present invention include the following:

Benzyl alcohol
Ethanol
Propanol
Isopropanol
Butanol, and structural isomers
Pentanol, and structural isomers
Hexanol, and structural isomers

The above acids and alcohols are readily available commercially, some of which are approved for pharmaceutical and food use, so some forms of HPMC film in accordance with the present invention is suitable for and approved for food and pharmaceutical use. Some HPMC film in accordance with the present invention is suitable for ingestion by humans. Some HPMC film in accordance with the present invention can thus be used for ingestible purposes, e.g. as wall material for ingestible delivery capsules.

The currently preferred acid plasticiser according to the present invention is maleic acid, with fumaric acid and then adipic acid being the next most favoured. In addition, benzyl alcohol has shown favourable characteristics for particular purposes.

It is preferred that the plasticiser is in the form of an acid or alcohol rather than a salt of the acid/alcohol, as the non salt form generally has better plasticising properties, (although salts including partial salts e.g. sodium and potassium salts of the acids/alcohols may be used, and in particular it may be convenient to use buffered casting solutions).

The acids, particularly maleic acid and alcohols, particularly benzyl alcohol, are also generally found to have good plasticising properties and to be capable of producing HPMC films with certain benefits and advantages as compared with HPMC films prepared using conventional plasticisers. These benefits and advantages include the following:

a) The film thermoforms very easily at lower temperatures and using less energy.
b) The deformed film retains its shape i.e. the film has no memory.
c) The film readily welds to itself and seals at lower temperatures using less heat and pressure.
d) The film tastes pleasant and has mouth watering effect.
e) The film has a high gloss appearance, improving the appearance of the finished product.

f) The plasticiser may comprise one or more materials, including one or more acids/alcohols and/or one or more salts of the acid/alcohol, possibly in combination with one or more other plasticisers such as those in the prior art e.g. polyethylene glycol, monopropylene glycol, glycerol and acetins.

The plasticiser is suitably present in an amount in the range of 2-40% by weight of the total weight of the film, typically about 23% by weight of the total weight of the film. One preferred film thus comprises about 23% maleic acid and about 77% by weight HPMC. Where a mixture of plastcisers is used, benefits may nevertheless be seen using an acid or alcohol according to the present invention, particularly maleic acid, at lower levels, say 5% by weight of the total weight of the film.

The film may include optional colourings, e.g. in the form of known food dyes such as FD and C yellow number 5, optional flavourings, artificial sweeteners, textures etc., in known manner.

The film may optionally be foamed, expanded or gasified, with small pockets of gas, e.g. air included in the film structure in known manner.

The minimum thickness of single ply unfoamed film, practically, would be 20 microns and the maximum thickness of single ply foamed film, practically, would be 300 microns.

The film typically has a thickness in the range 50-200 microns, e.g. in the range 60-130 microns, more preferably 70 - 90 microns, with the film thickness being controllable in known manner. Films of different thickness may be suited to different uses.

The film may be made in generally conventional manner, e.g. as described above, as is well known to those skilled in the art.

Film in accordance with the invention finds particular use as wall material for delivery capsules, as discussed above, particularly for ingestible

capsules. Other uses include, as biodegradeable packaging, water soluble sachets, carrier material for coating flavours (with flavour incorporated in the film or in coating on the film) for enrobing tablets etc.

In a further aspect, the invention further provides a delivery capsule having an enclosing wall comprising hydroxypropyl methyl cellulose film in accordance with the present invention.

Such delivery capsules may be made in generally conventional manner e.g. as disclosed in WO 97/35537, WO 00/27367 and WO 01/03676.

The invention will be further described, by way of illustration, in the following example.

Example.

A hydroxypropyl methyl cellulose film in accordance with the invention was made, having the following composition by weight:

Hydroxypropyl methyl cellulose	77%
Maleic acid	23%

The film was made in generally conventional manner. HPMC, in the form of powder, was mixed with maleic acid and water to produce an aqueous solution with stirring.
The composition of the HPMC casting solution was (%w:w) HPMC 10, water 87 maleic acid 3. The solution was deaerated by application of a vacuum. The solution was then fed into a feed hopper, including an elongate exit slot located a small distance above the upper surface of a moving conveyor belt to an end thereof, with the slot extending perpendicularly with respect to the direction of movement of the belt away from the feed hopper, forming a film. The film was passed on the belt through a heating zone in which hot air heated the film, driving off water and so drying the film. The resulting dried cast film was removed

from the belt and wound onto reels. The water content of the dried film was about 4% by weight, in the form of bound (non-free) water. The thickness of the dried film was about 120 microns.

The film has certain benefits and advantages as compared with films prepared using conventional plasticisers. These include the following:

a) The film thermoforms very easily at lower temperatures and using less energy.

b) The deformed film retains its shape i.e. the film has no memory.

c) The film readily welds to itself and seals at lower temperatures using less heat and pressure.

d) The film tastes pleasant and has mouth watering effect.

e) The film has a high gloss appearance, improving the appearance of the finished product.

The resulting film is suitable for human consumption, and one use is as a wall material for ingestible delivery capsules e.g. containing a dose of a pharmaceutical preparation or a dietary supplement. Such capsules may be made using known techniques, e.g. as described in WO 97/35537, WO 00/27367 and WO 01/03676.

Claims

1. A hydroxypropyl methyl cellulose film, comprising hydroxypropyl methyl cellulose plastcised with a plasticiser comprising an organic acid or a salt of an organic acid.

2. A film according to claim 1, wherein the plasticiser is a carboxylic acid.

3. A film according to claim 2 wherein, the plasticiser comprises one or more of maleic acid, fumaric acid, adipic acid.

4. A film according to claim 3 wherein the plasticiser comprises maleic acid.

5. A hydroxypropyl methyl cellulose film, comprising hydroxypropyl methyl cellulose plastcised with a plasticiser comprising an organic alcohol or a salt of an organic alcohol.

6. A film according to claim 5 wherein the plasticiser comprises the alcohol benzyl alcohol in combination with one or more of , maleic acid, fumaric acid, adipic acid.

7. A film according to claim 6 wherein the plasticiser comprises

benzyl alcohol.

8. A film according to claims 1,2,4,5, or 7 wherein the plasticiser is present in the amount in the range 5 to 40% by weight of the total weight of the film.

9. A film according to claims 4 or 7 comprising about 23% by weight of the plasticiser and 77% by weight of HPMC.

10. A film according to any one of the preceding claims, wherein the film is foamed, expanded or gasified.

11. A film according to any one of the preceding claims wherein the film has a thickness of between 50 to 200 microns.

12. A delivery capsule having an enclosing wall comprising a film in accordance with any one of the preceding claims.

13. A method of producing HPMC film suitable for forming into a capsule, comprising treating the HPMC film with acids and/or alcohols mentioned in any preceding claim, before and/or during when the film is manipulated to form a capsule.

INTERNATIONAL SEARCH REPORT

PCT/GB 03/01996

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C08L1/28 C08K5/092 C08K5/05 A61K9/48

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C08L A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
WPI Data, PAJ, CHEM ABS Data, EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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